Atty. Dkt. No. 041673-2047

Amendments to the Claims

This confirms Applicants' intention and request of October 12, 2005 to **amend** Claims 22, 30-31 and 33 as indicated below in the listing of claims.

Listing of Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Previously Presented) A method for ameliorating neuronal atrophy and loss in the mammalian brain, the method comprising delivering a neurotrophin-encoding transgene composition to preselected delivery sites in the brain for expression of neurotrophin at, or within diffusion distance of, targeted neurons, wherein the growth factor stimulates non-chemotropic growth by, or activity in, the targeted neurons.

2. (Cancelled)

3. (Cancelled)

4. (Cancelled)

5. (Cancelled)

6. (Withdrawn) The method according to Claim 1, wherein the neurotrophin-encoding transgene composition is delivered indirectly, from grafts of transgene-secreting donor cells introduced into the brain.

7. (Cancelled)

8. (Cancelled)

9. (Withdrawn) The method according to Claim 6, wherein the donor cells are delivered in a pharmaceutically acceptable composition having a concentration of at least 1 x 10^5 donor cells/μl.

10. (Withdrawn) The method according to Claim 9, wherein each graft contains from 2 to 20 μl of the donor cell containing composition.

11. (Cancelled)

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)

15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (Cancelled)

19. (Cancelled)

20. (Cancelled)

21. (Previously Presented) The method according to Claim 1, wherein the targeted neurons are cholinergic neurons.

22. (Currently Amended) The method according to Claim 21, wherein the stimulation occurs in a cortical region of the brain innervated by the targeted cholinergic neurons.

23. (Previously Presented) The method according to Claim 22, wherein each delivery site is preselected by correlating sites of potential loss of cortical fiber density to potential impairment of neurological function in the aging brain.

24. (Previously Presented) The method according to Claim 23, wherein the cortical region of the brain is the insular or temporal cortex.

25. (Previously Presented) The method according to Claim 22, wherein the stimulation occurs in the cingulate, frontal, entorhinal or hippocampal cortices.

26. (Previously Presented) The method according to Claim 21, wherein the stimulation occurs in the cholinergic forebrain.

27. (Previously Presented) The method according to Claim 22 or 26, wherein the region of the brain containing the targeted neurons is the striatum.

28. (Previously Presented) The method according to Claim 26, wherein the treated mammal is a human with Alzheimer's Disease.

29. (Previously Presented) The method according to Claim 1, wherein the targeted neurons are dopaminergic neurons.

30. (Currently Amended) The method according to Claim 29, wherein the stimulation occurs in dopaminergic neurons innervating the substantia nigra.

31. (Currently Amended) The method according to Claim 30, wherein the region of the brain containing the targeted dopaminergic neurons is the striatum.

32. (Previously Presented) The method according to Claim 29, wherein the treated mammal is a human with Parkinson's Disease.

33. (Currently Amended) A method for stimulating neuronal growth and activity in the mammalian brain, the method comprising delivering a neurotrophin-encoding transgene composition to a region of the brain having targeted neurons therein, wherein the expressed growth factor stimulates growth by, or activity in, ~~neurons in~~ the targeted neurons in another region of the brain innervated thereby.

34. (Previously Presented) The method according to Claims 1 or 33, wherein the growth factor-encoding transgene composition is delivered directly, by introduction of a transgene-expressing recombinant expression vector into the preselected delivery sites.

35. (Previously Presented) The method according to Claim 34, wherein the transgene-expressing recombinant expression vector is a viral vector.

36. (Previously Presented) The method according to Claim 35, wherein the viral vector is delivered in a pharmaceutically acceptable composition, and provides from 10^{10} to 10^{12} viral particles/ml of composition.

37. (Previously Presented) The method according to Claims 1 or 33, wherein the mammal is a human and the transgene encodes a human nervous system growth factor.

38. (Previously Presented) The method according to Claim 37, wherein the transgene encodes nerve growth factor (NGF).

39. (Previously Presented) The method according to Claim 1, wherein the transgene encodes neurotrophin 3 (NT-3).

40. (Previously Presented)) The method according to Claim 37, wherein the transgene encodes glial derived nerve growth factor (GDNF).

41. (Previously Presented) The method according to Claim 1, wherein the transgene encodes neurturin.

42. (Previously Presented) The method according to Claim 1, wherein the transgene encodes neurotrophin 4/5 (NT-4/5).

43. (Previously Presented) The method according to Claim 1, wherein the transgene encodes perspephin.

44. (Previously Presented) The method according to Claim 35, wherein the viral vector is an adeno-associated viral vector.

45. (Previously Presented) The method according to Claim 35, wherein the viral vector is a lentiviral vector.

46. (Previously Presented) The method according to Claim 1, wherein the mammal is a human with aging-related impairment.

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Clean Copy of the Amended Claims

1. A method for ameliorating neuronal atrophy and loss in the mammalian brain, the method comprising delivering a neurotrophin-encoding transgene composition to preselected delivery sites in the brain for expression of neurotrophin at, or within diffusion distance of, targeted neurons, wherein the growth factor stimulates non-chemotropic growth by, or activity in, the targeted neurons.

Claims 2 through 5 are cancelled.

Claim 6 is withdrawn.

Claims 7 and 8 are cancelled.

Claims 9 and 10 are withdrawn.

Claims 11 through 20 are cancelled.

21. The method according to Claim 1, wherein the targeted neurons are cholinergic neurons.

22. The method according to Claim 21, wherein the stimulation occurs in a cortical region of the brain innervated by the targeted cholinergic neurons.

23. The method according to Claim 22, wherein each delivery site is preselected by correlating sites of potential loss of cortical fiber density to potential impairment of neurological function in the aging brain.

24. The method according to Claim 23, wherein the cortical region of the brain is the insular or temporal cortex.

25. The method according to Claim 22, wherein the stimulation occurs in the frontal, cingulated, entorhinal or hippocampal cortices.

26. The method according to Claim 21, wherein the stimulation occurs in the cholinergic forebrain.

27. The method according to Claim 22 or 26, wherein the region of the brain containing the targeted neurons is the striatum.

28. The method according to Claim 26, wherein the treated mammal is a human with Alzheimer's Disease.

29. The method according to Claim 1, wherein the targeted neurons are dopaminergic neurons.

30. The method according to Claim 29, wherein the stimulation occurs in dopaminergic neurons innervating the substantia nigra.

31. The method according to Claim 30, wherein the region of the brain containing the targeted dopaminergic neurons is the striatum.

32. The method according to Claim 29, wherein the treated mammal is a human with Parkinson's Disease.

33. A method for stimulating neuronal growth and activity in the mammalian brain, the method comprising delivering a neurotrophin-encoding transgene composition to a region of the brain having targeted neurons therein, wherein the expressed growth factor stimulates growth by, or activity in, the targeted neurons in another region of the brain innervated thereby.

34. The method according to Claims 1 or 33, wherein the growth factor-encoding transgene composition is delivered directly, by introduction of a transgene-expressing recombinant expression vector into the preselected delivery sites.

35. The method according to Claim 34, wherein the transgene-expressing recombinant expression vector is a viral vector.

36. The method according to Claim 35, wherein the viral vector is delivered in a pharmaceutically acceptable composition, and provides from 10^{10} to 10^{12} viral particles/ml of composition.

37. The method according to Claims 1 or 33, wherein the mammal is a human and the transgene encodes a human nervous system growth factor.

38. The method according to Claim 37, wherein the transgene encodes nerve growth factor (NGF).

39. The method according to Claim 1, wherein the transgene encodes neurotrophin 3 (NT-3).

40. The method according to Claim 37, wherein the transgene encodes glial derived nerve growth factor (GDNF).

41. The method according to Claim 1, wherein the transgene encodes neurturin.

42. The method according to Claim 1, wherein the transgene encodes neurotrophin 4/5 (NT-4/5).

43. The method according to Claim 1, wherein the transgene encodes perspephin.

44. The method according to Claim 35, wherein the viral vector is an adeno-associated viral vector.

45. The method according to Claim 35, wherein the viral vector is a lentiviral vector.

46. The method according to Claim 1, wherein the mammal is a human with aging-related impairment.